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5370 Manhattan Circle Suite 201
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EXAMINER

FOX, DAVID T

ART UNIT	PAPER NUMBER
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1638

DATE MAILED: 05/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/936,869	Applicant(s) PODILA ET AL.	
	Examiner David T. Fox	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-30 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-30 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>3/29/02; 4/12/02</u> | 6) <input type="checkbox"/> Other: ____ |

The application should be reviewed for errors. Errors appear, for example, on page 4 of the instant specification, line 5, where "mads" should be replaced with ---MADS---. See page 5, line 12 of the New Zealand priority document.

In addition, page 20 of the instant specification, line 20 defines the PrAG1 promoter as "1.46 kb, sequence of Figure 2". However, Figure 2 is only 1401 base pairs long. Clarification is requested. New matter should be avoided.

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim 8 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend upon another multiple dependent claim, i.e. claims 6-7. See MPEP § 608.01(n). In the interest of compact prosecution, the claim has been treated on the merits. Such treatment does not relieve Applicant of the responsibility to respond to this objection.

Claims 8 and 24 are objected to under 37 CFR 1.821(d) for employing incorrect sequence identifiers. Claim 8 refers to a peptide "having SEQ ID NO:3"; however, SEQ ID NO:3 is a gene, not a peptide. Replacement of "3" with ---4--- would obviate this objection. Similarly, claim 24 refers to an RNase (a protein) which "has the sequence of SEQ ID NO:5". Since SEQ ID NO:5 is a gene, while SEQ ID NO:6 is a protein, claim 24 should be amended to replace "5" with ---6---.

Claims 27 and 30 are objected to for employing improper Markush terminology. See MPEP 2173.05(h). In line 2 of each claim, ---the group consisting of--- should be inserted after "from".

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35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-3 are rejected under 35 U.S.C. 101 because the claimed invention is not statutory subject matter.

The DNA molecules as claimed have the same characteristics and utility as those found naturally in the genome or as cellular precursors thereof and therefore do not constitute patentable subject matter. See *American Wood v. Fiber Distintegrating Co.*, 90 U.S. 566 (1974), *American Fruit Growers v. Brogdex Co.*, 283 U.S. 2 (1931), *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 33 U.S. 127 (1948), *Diamond v. Chakrabarty*, 206 USPQ 193 (1980).

Amendment of claims 1-3 to replace "A" in line 1 with ---An isolated--- would obviate this rejection.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 4-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Dependent claims are included in all rejections.

Claim 1 is indefinite in its recitation of "that nucleotide sequence" in line 3, as it is unclear whether this refers to SEQ ID NO:1 or to a nucleotide sequence encoding a peptide.

Claim 1 is further indefinite in its recitation of "thereof" in line 4, as it is unclear whether this refers to the promoter or the coding sequence.

Claims 4-5 are indefinite for failing to clearly specify the relationship between the claim elements. Insertion of the phrase ---as operably linked components--- in line 1 of each claim, after "comprises", would obviate this rejection.

Claim 5 is indefinite in its recitation in part (a) of "90% homology...as given in SEQ ID NO:2" as it is unclear whether the promoter has 90% homology to SEQ ID NO:2 or whether the promoter has SEQ ID NO:2.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2 and 4-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a promoter comprising a polynucleotide of any length and any sequence and from any source, which is a "functionally equivalent variant" of SEQ ID NO:1, or a polynucleotide with at least 90% homology to SEQ ID NO:1, or a polynucleotide which has the nucleotide sequence of SEQ ID NO:1, which comprises base pairs 1-1320 of Figure 2; and plants transformed therewith. However, the specification only

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provides guidance for a promoter which comprises at least nucleotides 1-1401 of Figure 2, i.e. SEQ ID NO:2. No guidance is provided for any variant, subsequence or functional equivalent of SEQ ID NO:2 which functions as a promoter.

The Federal Circuit has recently clarified the application of the written description requirement. The court stated that a written description of an invention "requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1568; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The court also concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." *Id.* Further, the court held that to adequately describe a claimed genus, Patent Owner must describe a representative number of the species of the claimed genus, and that one of skill in the art should be able to "visualize or recognize the identity of the members of the genus." *Id.*

See MPEP Section 2163, page 156 of Chapter 2100 of the August 2001 version, column 2, bottom paragraph, where it is taught that

[T]he claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.

Given the claim breadth and lack of guidance as discussed above, the specification fails to provide an adequate written description of the genus of sequences as broadly claimed. Given the lack of written description of the claimed genus of sequences, any method of using them, such as transforming plant cells and plants therewith, and the resultant products including the claimed transformed plant cells and plants containing the genus of sequences, would also be inadequately described. Accordingly, one skilled in the art would not have recognized Applicant to have been in possession of the claimed invention at the time of filing. See the Written Description Requirement guidelines published in Federal Register/ Vol. 66, No. 4/ Friday January 5, 2001/ Notices: pp. 1099-1111.

See also *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at 1021, (Fed. Cir. 1991) where it is taught that a gene (which includes a promoter) is not reduced to practice until the inventor can define it by "its physical or chemical properties" (e.g. a DNA sequence).

See also *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

Claims 1-2 and 4-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited to the entire promoter fragment of the PrAG1 gene from *Pinus radiata*, i.e. SEQ ID NO:2, constructs comprising the promoter operably linked to a heterologous sense gene encoding a peptide which

causes cell death, and plants transformed therewith for the production of sterile plants; does not reasonably provide enablement for claims broadly drawn to any fragment or variant or functional equivalent of SEQ ID NO:2, or for claims broadly drawn to constructs comprising the sense PrAG1 coding sequence or any antisense coding sequence, for the production of sterile plants. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1-2 and 4-30 are broadly drawn to a promoter comprising a polynucleotide of any length and any sequence and from any source, which is a "functionally equivalent variant" of SEQ ID NO:1, or a polynucleotide with at least 90% homology to SEQ ID NO:1, or a polynucleotide which has the nucleotide sequence of SEQ ID NO:1, which comprises base pairs 1-1320 of Figure 2; and plants transformed therewith. Figure 2 is characterized as the sequence of the promoter of an AGAMOUS gene from *Pinus radiata*, which is preferentially expressed in reproductive tissues. However, the specification only provides guidance for a promoter which comprises at least nucleotides 1-1401 of Figure 2, i.e. SEQ ID NO:2, which functions as a reproductive tissue-specific promoter. No guidance is provided for any variant, subsequence or functional equivalent of SEQ ID NO:2 which functions as a promoter, either constitutive or tissue-specific.

Furthermore, claims 4-11 and 16 are drawn to constructs comprising a promoter and any gene in sense or antisense orientation, including a gene encoding the PrAG1

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polypeptide of SEQ ID NO:4, for the production of sterile plants. Claims 10, 16 and 22 are drawn to constructs which cause the conversion of reproductive structures into vegetative structures, or which alter the timing of flowering, and plants transformed therewith. However, the specification only provides guidance for constructs comprising the exemplified promoter operably linked to a heterologous sense gene encoding a protein which confers cell death, including a ribonuclease, for the production of sterile plants. No guidance is provided regarding the identification, isolation or evaluation of any sequences which somehow convert reproductive structures such as stamens into vegetative structures such as leaves. No guidance is provided regarding the identification, isolation or evaluation of any sequences which accelerate or delay flowering time. No guidance is provided regarding the evaluation or obtention of sterile plants following plant transformation with any antisense RNA-encoding construct, or with any sense construct encoding a MADS-box protein such as PrAG1.

The modification of promoter sequence and subsequent retention of constitutive or tissue-specific promoter function is unpredictable. Birren et al teach a derivative of SEQ ID NO:1, with 50.3% local similarity thereto, which is a mouse sequence and clearly not a plant AGAMOUS promoter.

Kim et al teach the extreme sensitivity of promoter regions to single base pair changes, the absolute requirement for as few as 3 to 6 nucleotides for promoter function, and the failure of a promoter to function either constitutively or specifically when lacking oligonucleotide regions approximately 100 bp upstream of the

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transcription start site (see Kim et al., page 106, paragraph bridging the columns; paragraph bridging pages 107 and 108; page 110, paragraph bridging the columns).

Furthermore, tissue-specific gene expression could be the result of a variety of complex factors other than a tissue-specific promoter immediately upstream of the structural gene. Such alternate factors include distant genes encoding regulatory proteins, activator/operator/repressor systems, far upstream or downstream enhancer elements, changes in the phosphorylation of transcriptional proteins, export of mRNA from DNA found in other organelles or tissues, transposable elements, and post-transcriptional controls such as alternative RNA splicing (see, e.g., *Molecular Biology of the Cell*, pages 553-569; 588-597, and 606-607).

Thus, multiple attempts to isolate the putatively tissue-specific promoters associated with a multitude of genes encoding tissue-specific gene products could prove unsuccessful.

Furthermore, promoters from other AGAMOUS homologues may be insufficient to confer reproductive tissue-specific expression, which specificity would be required to induce sterility while avoiding toxic effects in the rest of the plant. Rottmann teaches that AGAMOUS promoters generally share little sequence similarity and so would be difficult to isolate, and also teaches that known AGAMOUS promoters are insufficient to confer reproductive tissue-specific expression (see, e.g., column 4, lines 21-41; column 27, lines 65-67).

In addition, plant transformation with sense or antisense genes which are reproductive tissue-specific, or which are MADS box protein-encoding genes such as the *Pinus radiata* AGAMOUS gene encoding SEQ ID NO:4, is unpredictable and

unlikely to confer sterility or other changes in flowering structure or behavior. Turgut et al failed to obtain male sterile plants following transformation with a DNA construct comprising a highly pollen-specific promoter and an antisense gene theorized to destroy pollen development or function (see, e.g., page 97, Abstract). Roberts et al teach that plant transformation with a construct comprising an anther-specific promoter operably linked to a ribonuclease gene failed to eliminate the production of viable pollen (see, e.g., page 299, Abstract). Rottmann teaches that plant transformation with sense genes encoding MADS box proteins such as AGAMOUS may result in cosuppression of these genes in vegetative organs, thus harming overall plant health (see, e.g., column 4, lines 42-51).

Furthermore, plant transformation with AGAMOUS homologues in sense orientation failed to produce sterile plants, plants without reproductive structures, plants where reproductive structures had been converted into vegetative structures, or plants with altered flowering times. Rutledge et al (1998, The Plant Journal) teach that plant transformation with an AGAMOUS homologue from black spruce produced flowers with two whorls of stamens—the original whorl of stamens as well as a whorl of stamens where petals would normally occur (see, e.g., pages 626, 628 and 629). Mouradov et al also teach that plant transformation with a gene encoding a MADS box protein produced plants with flowers comprising two whorls of stamens (see, e.g., page 245, column 2; page 246, column 1, top paragraph).

Given the claim breadth, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to identify, isolate and evaluate the following for promoter activity, either constitutive or reproductive tissue-specific: a multitude of truncations of SEQ ID NO:2 including SEQ ID NO:1, a multitude of sequences with at least 90% homology to SEQ ID NO:1, or a

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multitude of "functional equivalents" of SEQ ID NO:1 which are derived from any plant species and are of any length and sequence. Furthermore, undue experimentation would have been required to identify, isolate and evaluate a multitude of non-exemplified sequences in sense or antisense orientation for their ability to cause sterility, change in flowering time, or conversion of reproductive organs into vegetative organs in plants transformed therewith.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 4, 6, 9 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Tandre et al (1998) in light of Tandre et al (1995).

The claims are drawn to a promoter which is a functionally equivalent variant of a *Pinus radiata* AGAMOUS gene promoter, DNA constructs comprising the promoter operably linked to an open reading frame in sense orientation, wherein said open reading frame causes abortion of reproductive structures.

Tandre et al (1998) teach genomic clones of a Norway spruce AGAMOUS homologue, wherein said genomic clones contain both the reproductive tissue-specific promoter and the coding sequence, and wherein the expression of the coding sequence

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causes the abortion of reproductive organs as evidenced by loss of seed set and failure of reproductive organs to develop in their usual location (see, e.g., page 615, paragraph bridging the columns; page 616; page 617, top paragraph of each column; paragraph bridging pages 617 and 618; page 618, column 2, bottom paragraph; page 619, column 2, first full paragraph; page 621, column 2, bottom paragraph). The AGAMOUS promoter from Norway spruce is a functional equivalent of the AGAMOUS promoter from *Pinus radiata*, particularly in view of the 88.6% local similarity thereto as demonstrated by Tandre et al (1995, Accession No. PADAL2).

Claims 1-2, 4, 6-7, 9-14, 16 and 21-23 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 98/13503 (F.B. INVESTMENTS).

The claims are drawn to a promoter which is a functionally equivalent variant of a *Pinus radiata* AGAMOUS gene promoter, DNA constructs comprising the promoter operably linked to an open reading frame in sense orientation or antisense orientation; wherein said open reading frame causes conversion of reproductive structures to vegetative structures, alterations in flowering time or abortion of reproductive structures; and wherein said open reading frame includes a ribonuclease-encoding gene including the barnase gene.

F.B. INVESTMENTS teaches *Pinus radiata* and *Eucalyptus grandis* genes encoding MADS box-containing proteins, wherein said genes are preferentially expressed in reproductive structures, and wherein the expression of promoters of these genes operably linked to either the coding sequence in antisense orientation or a barnase gene in sense orientation leads to abortion of reproductive structures,

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conversion of reproductive structures into vegetative structures, and total delay in flowering time (i.e. flowering does not occur). See, e.g., pages 1-5, 7, 14-18, 20, 23-24 and 28-29; and Figures 12, 15, 21a, 33-34, 43 and 46. Given the similar gene products, the similar expression patterns, and the similar effects, the promoters taught by F.B. INVESTMENTS are functionally equivalent variants of the *Pinus radiata* AGAMOUS promoter of SEQ ID NO:1.

Claims 1-2, 4, 6-7, 9-14, 16 and 21-23 are rejected under 35 U.S.C. 102(e) as being anticipated by Strauss et al (US 6,395,892 effectively filed April 6, 1998).

Strauss et al teach a poplar AGAMOUS promoter which is a functionally equivalent variant of the *Pinus radiata* AGAMOUS promoter of SEQ ID NO:1, said poplar AGAMOUS promoter ligated to an open reading frame encoding a MADS box-containing protein in antisense orientation or an open reading frame encoding a cytotoxic protein such as barnase in sense orientation, wherein plant transformation therewith leads to plants with completely delayed flowering (i.e. no flowering), plants with aborted reproductive organs, and plants where the reproductive organs have been replaced by vegetative organs (see, e.g., column 4, lines 16-26; columns 6-7; columns 14-19 and 21-22; SEQ ID NOS: 9 and 13; and claims 14-24 and 26).

Claims 3, 5, 8, 15, 17-20 and 24-30 are deemed free of the prior art, given the failure of the prior art to teach or reasonably suggest an isolated promoter with at least 90% homology to SEQ ID NO:1 or plants transformed therewith, the failure to suggest plant transformation with said promoter operably linked to the *Arabidopsis* RNase2

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gene encoding SEQ ID NO:6, and the failure to suggest plant transformation with said promoter operably linked to the coding sequence of SEQ ID NO:3.

No claim is allowed.

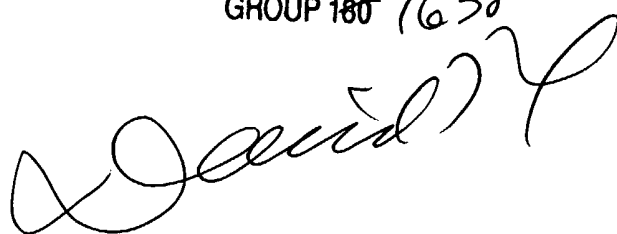
Any inquiry concerning this communication or earlier communications from the examiner should be directed to David T. Fox whose telephone number is (571) 272-0795. The examiner can normally be reached on Monday through Friday from 10:30AM to 7:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on (571) 272-0804. The fax phone number for this Group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

May 19, 2004

DAVID T. FOX
PRIMARY EXAMINER
GROUP 180 1638

A handwritten signature in black ink, appearing to read "David T. Fox", written over the printed name and title.